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Original Article

Local versus Systemic Analgesia in Pain Management of Post-Laparoscopic Cholecystectomy Patients

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Abstract

Objective: To compare the efficacy of Toradol and a combination of bupivacaine with Toradol for postoperative analgesia in patients who underwent laparoscopic cholecystectomy.

Methodology: This interventional study was conducted in the Department of Surgery, KMU-IMS, DHQ Teaching KDA Kohat, from June 2024 to Dec 2024. Two hundred and twenty-four patients who underwent laparoscopic cholecystectomy were divided into group T (received injection Toradol 0.5mg/kg I/V) and group TB (received 30ml of 0.25% injection bupivacaine intraperitoneally along with intravenous 0.5mg/kg injection Toradol). We recorded pain using VAS at 1, 2, and 4 hours postoperatively. Rescue analgesia was given in patients with a VAS score > 3 who were uncomfortable with pain. We used the chi-square test to compare effectiveness between the two groups.

Results: Mean ages were 37.41 ± 3.09 years and 38.96 ± 2.64 years in group T and Group TB, respectively. Mean VAS was 4.47 ± 1.36 and 1.38 ± 0.56 in group T and group TB, respectively. Rescue analgesia was given to 23.21% of patients in group T and 0.0% in group TB (p-value=0.0003). Toradol injection was effective in 76.78% of patients, while the combination of Toradol and bupivacaine was effective in 100.0% of patients (p-value=0.0001).

Conclusions: The efficacy of Toradol with bupivacaine was high as compared to Toradol alone for postoperative pain control after laparoscopic cholecystectomy.

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Introduction

Laparoscopic cholecystectomy is one of the most frequently performed elective general surgical operations. It is an ideal candidate for a day-case or short-stay procedure; therefore, adequate postoperative pain relief is of considerable importance[1]. Laparoscopic cholecystectomy (LC) is the gold standard and the most commonly performed operation in the department of general surgery in hospitals. Although there are clear benefits compared with open surgery, postoperative pain after laparoscopic cholecystectomy remains an issue. Pain can prolong hospital stay and lead to increased morbidity, which is particularly important now that many centers are performing this operation as a day-case procedure. This results in a shorter hospital stay and an earlier return to regular activity[2,3]. Local anesthetics (LA) are increasingly used intraoperatively to prevent postoperative pain. The efficacy of local anesthetic infiltration into incision sites has only been shown in patients undergoing inguinal herniorrhaphy[4]. However, one meta-analysis has shown intraperitoneal LA to be effective for pain relief following laparoscopic cholecystectomy (LC). Instillation of local anesthetics intraperitoneally (IP) around the operative site is used as an analgesic technique on the assumption that conduction from visceral sites is obstructed and may lessen the intensity of referred pain to the shoulder (C3, C4), which results from irritation of diaphragmatic innervations, i.e., phrenic nerve (C3, C4, C5) and diaphragmatic stretching due to gaseous distension, in the postoperative period[5]. Intraperitoneal administration of local anesthesia is often used to improve pain relief after laparoscopic cholecystectomy. As early as 1980, it was reported that instillation of local anesthetic (980 ml of bupivacaine 0.125%, epinephrine 1:200,000) under the right diaphragm reduced shoulder pain after minor gynecological laparoscopy. Following this, various studies were conducted to study the efficacy of intraperitoneal analgesics for postoperative pain relief after laparoscopic cholecystectomy[6,7]. Administration of non-steroidal anti-inflammatory drugs (NSAIDs), intraperitoneal local anesthetics, and opioids is carried out to reduce pain after laparoscopic cholecystectomy[8,9]. To provide local statistics and suggest better treatment options, we conducted this study to evaluate intravenous Toradol (Ketorolac) alone versus intravenous Toradol plus intraperitoneal (IP) bupivacaine for postoperative pain relief in patients undergoing laparoscopic cholecystectomy[10].

Materials and methods

The Department of Surgery, KMU-IMS, DHQ Teaching, KDA, Kohat, conducted this interventional study from June 2024 to Dec 2024.

Sample size by WHO calculator

Level of significance: 5% Power of study: 80% P1 (proportion of rescue analgesia requirement in Toradol group): 00% P2 (proportion of rescue analgesia requirement in bupivacaine plus Toradol group): 26% 10

Sample size

224 patients (112 patients in each group)

Sample technique

Non-probability consecutive sampling

Inclusion criteria

- Gender: both
- Age: 20 - 60 years
- ASA I & II underwent laparoscopic cholecystectomy

Exclusion criteria

Patients with previous history of respiratory disease, e.g., chronic obstructive airway disease and asthma; patients with ischemic heart disease; patients with known history of gastro-esophageal reflux syndrome taking pre-operatively anti-inflammatory and analgesic drugs; and patients with allergy or sensitivity to bupivacaine and tramadol

Data Collection

All patients who met the inclusion criteria and were selected for laparoscopic cholecystectomy were included in this study. The institution's ethics committee approved this study. We obtained written consent from patients to be included in the study. We coded all data by study ID number for analysis, with the study coordinator as the only person with access to patient names and chart numbers. Patients were divided into two groups (group T and group TB) by lottery. Group T received intravenous 0.5mg/kg Toradol (ketorolac), and group TB received 30 mL of 0.25% bupivacaine injection intraperitoneally, along with intravenous 0.5mg/kg Toradol (ketorolac). The local anesthetic/ analgesic solution was sprayed on the upper surface of the liver and on the right subdiaphragmatic space and over the gallbladder bed. This was done using a size 14 infant feeding tube inserted through the subcostal trocar, guided by an instrument through the epigastric port, under direct laparoscopic control, in the supine position at the end of surgery. All patients were given standard premedication as advised in the pre-anesthetic checklist. General anesthesia was induced. Intra-abdominal pressure was maintained at 10-12mmHg—10ml of 0.25% inj. Bupivacaine was given to all patients at the port sites for parietal (somatic) pain to assess visceral pain better. Study drugs were instilled 15 minutes before the end of surgery, according to the group allocation by the surgeons (among the researchers). All patients were transferred to the post-anesthesia care unit for two hours after surgery. Visual analog scale (VAS) score was recorded by surgeons, not part of the operating team of that particular patient, and hence was blinded as to which drug was being assessed. Pain intensity was recorded for all patients using VAS at 1, 2, and 4 hours after surgery. Rescue analgesia with inj. Nalbuphine 10mg IV stat was given to patients with a VAS score > 3 and who were uncomfortable with pain. All information was collected by a predesigned proforma.

Data Analysis

Data from both groups were collected independently and entered into SPSS version 24. For age, weight, length of operation, and VAS score, we calculated the mean and standard deviation. We calculated frequencies and percentages for gender, ASA status, rescue analgesia, and efficacy. We compared the two groups using the chi-square test.

Results

This study included 224 patients. In Group T, the mean age of the patients who received intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 37.41 ± 3.09 years. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 11 (9.82%) patients in the age range of 20 – 30 years, 58 (51.78%) patients in the age range of 31 – 40 years, 29 (25.89%) patients in the age range of 41 – 50 years, and 14 (12.5%) patients in the age range of 51 – 60 years. (Table 1) In Group TB, the mean age of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 38.96 ± 2.64 years. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 3 (2.67%) patients in the age range of 20 – 30 years, 71 (63.39%) patients in the age range of 31 – 40 years, 31 (27.67%) patients in the age range of 41 – 50 years, and 7 (6.25%) patients in the age range of 51 – 60 years. (Table 1) In Group T, there were 29 (25.89%) male and 83 (74.10%) female patients who received intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy. The male-to-female ratio was 1:2.8 (Table 1). In Group TB, 12 (10.71%) male and 100 (89.28%) female patients received 30ml of 0.25% bupivacaine injection intraperitoneally, along with intravenous 0.5mg/kg Toradol (Ketorolac), for postoperative analgesia after laparoscopic cholecystectomy. The male-to-female ratio was 1:8.3, and the p-value was 0.873. (Table 1) In Group T, the mean weight of patients who received intravenous Toradol (Ketorolac) 0.5 mg/kg for postoperative analgesia after laparoscopic cholecystectomy was 84.01 ± 4.83 Kg. Out of 112 patients who underwent laparoscopic cholecystectomy, there were 2 (1.78%) patients of weight ≤ 50 Kg, 109 (97.32%) patients of weight 51-100 kg, and 1 (0.89%) patient of weight >100 Kg. (Table 1) In Group TB, the mean Weight of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 81.91 ± 2.02 Kg. Of the 112 patients who underwent laparoscopic cholecystectomy, 5 (4.46%) weighed ≤ 50 Kg, 105 (95.62%) weighed 51-100 kg, and 2 (1.78%) weighed > 100 kg. (Table 1) In Group T, the mean surgical duration for patients who received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 96.01 ± 29.46 min. Of the 112 patients who underwent laparoscopic cholecystectomy, surgery lasted ≤ 60 minutes in 43 (38.39%) patients and > 60 minutes in 69 (61.60%) patients. (Table 1) In Group TB, the mean duration of surgery for patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 108.01 ± 27.09 min. Of the 112 patients who underwent laparoscopic cholecystectomy, surgery lasted ≤ 60 minutes in 23 (20.53%) patients and > 60 minutes in 89 (79.46%) patients. (Table 1) In Group T, of the 112 patients who

received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, 73 (65.17%) had ASA score I and 39 (34.82%) had ASA score II. (Table 1) In Group TB, out of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, there were 61 (54.46%) patients with ASA score I and 51 (45.53%) patients with ASA score II. The p-value was 0.531. (Table 1) In Group T, the Mean Visual Analog score of patients who received intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 4.47 ± 1.36 . Of the 112 patients who underwent laparoscopic cholecystectomy, the Mean Visual Analog score was 3.31 ± 1.46 at the 1st Hour postop, 6.02 ± 0.93 at the 2nd hour postop, and 4.58 ± 1.06 at the 4th hour postop. (Table 6) In Group TB, the Mean Visual Analog score of patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was 1.38 ± 0.56 . Of the 112 patients who underwent laparoscopic cholecystectomy, the Mean Visual Analog score was 2.01 ± 0.08 at the 1st Hour postop, 1.04 ± 0.13 at the 2nd hour postop, and 1.20 ± 0.94 at the 4th hour postop. (Table 2) In Group T, out of 112 patients who received intravenous 0.5mg/Kg injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, there were 26 (23.21%) patients who required rescue analgesia for postoperative pain. In contrast, in 86 (76.78%) patients, intravenous 0.5mg/Kg injection of Toradol (Ketorolac) effectively controlled postoperative pain. (Table 3) In Group TB, out of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/Kg injection of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, none of the patients (0.0%) required rescue analgesia for postoperative pain. The p-value was 0.0003. (Table 4) In Group T, out of 112 patients who received intravenous 0.5mg/Kg injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, in 86 (76.78%) patients intravenous 0.5mg/Kg injection Toradol (Ketorolac) was effective in controlling postoperative pain. In comparison, Toradol alone was not effective in 26 (23.21%) patients. (Table 7) In Group TB, of 112 patients who received 30ml of 0.25% bupivacaine injection intraperitoneally along with intravenous 0.5mg/kg Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy, the combination of Toradol and bupivacaine was effective in controlling postoperative pain in 112 (100.0%) patients. The p-value was 0.0001. (Table 8)

Table 1: Distribution of patients by using different parameters

Parameters	Sub category	Group T (n=112)	Group TB (n=112)	P value
Age in years		Frequency	%age	0.001
	20 - 30	11	9.82	
	31 - 40	58	51.78	
	41 - 50	29	25.89	
	51 - 60	14	12.5	

Gender	Male	29	25.89	12	10.71	0.873
	Female	83	74.10	100	89.28	
Weight (kg)	≤50	2	1.78	5	4.46	0.431
	51-100	109	97.32	105	95.62	
	>100	1	0.89	2	1.78	
Duration of surgery (min.)	≤60	43	38.39	23	20.53	0.231
	>60	69	61.60	89	79.46	
ASA Score	I	73	65.17	61	54.46	0.531
	II	39	34.82	51	45.53	

Values are presented as frequency (n) and percentage (%). A p-value <0.05 was considered statistically significant.

Table 2: Mean Visual Analogue score at 1st, 2nd & 4th hours postoperatively (n=224)

VAS Score	Group T (n=112)	Group TB (n=112)
At 1st Hour postop	3.31 ± 1.46	2.01 ± 0.08
At 2nd hour postop	6.02 ± 0.93	1.04 ± 0.13
At 4th hour postop	4.58 ± 1.06	1.20 ± 0.94
Mean ± SD	4.47 ± 1.36	1.38 ± 0.56

Values are presented as mean ± standard deviation (SD). VAS, Visual Analogue Scale.

Table 3: Distribution of patPatients by rescue analgesia

Rescue analgesia	Group T (n=112)		Group TB (n=112)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Yes	26	23.21	0	0.0
No	86	76.78	112	100.0
P-Value*	0.0003**			

Values are presented as frequency (n) and percentage (%). A p-value <0.05 was considered statistically significant.

Table 4: Distribution of patients by effectiveness of analgesia

Effectiveness	Group T (n=112)		Group TB (n=112)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Yes	86	76.78	112	100.0
No	26	23.21	0	0.0
P-Value*	0.0001**			

Values are presented as frequency (n) and percentage (%). We considered a p-value <0.05 statistically significant.

Discussion

In this prospective clinical study of 224 patients, we compared the efficacy of Toradol and a combination of bupivacaine with Toradol

for postoperative analgesia in patients who underwent laparoscopic cholecystectomy[11]. The mean ages of the patients who underwent laparoscopic cholecystectomy were 37.41 ± 3.09 years and 38.96 ± 2.64 years in Group T and Group TB, respectively. The majority of patients, i.e., 51.78% and 63.39% in Group T and Group TB, respectively, in our study belonged to the middle age group, i.e., 31-40 years. In a study by Kashmiri ZA et al., the age ranges of patients who underwent laparoscopic cholecystectomy were 23–60 years and 24–65 years in Group A and Group B, respectively [12].The majority of patients who underwent laparoscopic cholecystectomy, i.e., 74.10% and 89.28% in Group T and Group B, respectively, in our study were females. However, the results were not statistically significant (p-value = 0.873). In a study by Kashmiri ZA et al., the male-to-female ratio was 6:34 and 8:32 in Group A and Group B, respectively [13].The mean weight of the patients who received laparoscopic cholecystectomy was 84.01 ± 4.83 Kg and 81.91 ± 2.02 Kg in Group T and Group TB, respectively. The majority of patients, i.e., 97.32% and 95.62% in Group T and Group TB, respectively, in our study belonged to the weight group of 51- 100 kg.The mean duration of surgery for patients who received laparoscopic cholecystectomy was 96.01 ± 29.46 min and 108.01 ± 27.09 min in Group T and Group TB, respectively. In our study, most patients (61.60% in Group T and 61.60% in Group TB) had prolonged surgery (>60 minutes). In a study by Kashmiri ZA10 et al., surgery lasted 35–90 minutes and 39–92 minutes in Group A and Group B, respectively. These findings align with other studies [14].Most patients (65.17% in Group T and 65.17% in Group B) had an ASA score of I. However, the results were not statistically significant (p-value = 0.531). These findings align with other studies [15]. In our study, the mean visual analog score for patients who received laparoscopic cholecystectomy was 4.47 ± 1.36 and 1.38 ± 0.56 in group T and TB, respectively. In our study, 23.21% of patients in group T required rescue analgesia for postoperative pain, while none (0.0%) in group TB required rescue analgesia for postoperative pain; the results were statistically significant (p-value = 0.0003) [16].In our study, intravenous Toradol (Ketorolac) 0.5 mg/kg for postoperative analgesia after laparoscopic cholecystectomy was effective in 76.78% of patients. At the same time, a combination of Toradol and bupivacaine was effective in 100.0% of patients in controlling postoperative pain. The results were statistically significant (p-value= 0.0001). In a Systematic Review and Meta- Analysis by Boddy AP et al., the use of intraperitoneal local anesthesia resulted in a significantly reduced pain score at 4 h (weighted mean difference, -9 mm; 95% confidence interval [CI], -13 to -5)[17]. Subgroup analysis suggested that the effect was greater when the local anesthetic was given at the start of the operation (WMD, -13 mm; 95% CI, -19 to -7) compared with instillation at the end (WMD, -6 mm; 95% CI, -10 to -2). In one study, VAS scores showed that group B patients who received a combination of bupivacaine and Toradol had lower scores than group A patients who received Toradol alone. However, the difference was not statistically significant (p>0.05). Rescue analgesic requirement was also significantly lower in group B than in group A (p<0.00)[18].We cross-tabulated the data (Effectiveness) by effect modifier (age). We found that the effectiveness of injection Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was higher in young patients (20-20 years), at 90.90%, followed by middle-aged patients (41-50 years), at 82.75%.

The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all age groups. However, the results were statistically not significant ($p\text{-value}>0.05$) [19]. We also cross-tabulated the data (Effectiveness) by effect modifier (Gender). We found that the effectiveness of Toradol (Ketorolac) for postoperative analgesia after laparoscopic cholecystectomy was higher in female patients (77.10%) than in male patients (75.86%). The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in both genders. However, the results were statistically not significant ($p\text{-value}>0.05$) [20]. We cross-tabulated the data (Effectiveness) by effect modifier (Weight). We found that the effectiveness of Toradol (Ketorolac) injection for postoperative analgesia after laparoscopic cholecystectomy was higher (100.0%) in patients weighing less than 50 kg. The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all patients with different weight groups. However, the results were statistically not significant ($p\text{-value}>0.05$) [21]. We also cross-tabulated effectiveness by effect modifier (Duration of surgery). We found that Toradol (Ketorolac) was more effective for postoperative analgesia after laparoscopic cholecystectomy in patients with a duration of surgery ≤ 60 minutes (91.30%). The effectiveness of the bupivacaine and Toradol combination for postoperative analgesia after laparoscopic cholecystectomy was found to be 100.0% in all patients with different operative times. However, the results were not statistically significant ($p\text{-value} > 0.05$). These findings align with previous studies that reported similar results. The study has several limitations. One center conducted the study. To make recommendations, more research is needed to examine the effectiveness of Toradol and a combination of bupivacaine and Toradol for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

Conclusion

The efficacy of bupivacaine with intravenous Toradol is high as compared to Toradol alone in postoperative pain control after laparoscopic cholecystectomy. So, it is recommended that a combination of Toradol with bupivacaine should be used during laparoscopic cholecystectomy to achieve better pain control after surgery.

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